

Application No. 09/582,719  
Amendment Dated December 2, 2004  
Reply to Office Action of June 2, 2004

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Currently Amended) An isolated and purified polynucleotide encoding the sequence Sequence of a human beta2-adrenergic receptor gene according to SEQ ID NO: 1, the sequence comprising at least one base substitution at one or more positions selected from the group consisting of positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, 1839, 2110, 2640 and 2826.
2. (Withdrawn) Sequence according to claim 1 wherein it involves completely or partly the substitution of bases T -> A (position 159), A -> G (position 245), G -> A (position 565), G -> A (position 934), G -> C (position 1120), C -> T (position 1221), C -> T (position 1541), T -> C (position 1568), A -> G (position 1633), C -> G (position 1666), G -> A, (position 1839), C -> T (position 2078), C -> A (position 2110), G -> C (position 2640) and G -> A (position 2826).
3. (Currently amended) Sequence according to claim 1 characterized by the mutations wherein residue 1541 is a T 1541-T, residue 1633 is an A and residue 1666 is a C.
4. (Withdrawn) Sequence according to claim 1 characterized by the mutations 1541 C, 1633 G and 1666 G.
5. (Withdrawn) Sequence according to claim 1 characterized by the mutations 1541 T, 1633 G and 1666 C.

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6. (Withdrawn) Sequence according to claim 1 characterized by the mutations 1541 T, 1568 T, 1633 A and 1666 C.
7. (Withdrawn) Sequence according to claim 1 characterized by the mutations 1541 C, 1568 C, 1633 G and 1666 G.
8. (Withdrawn) Sequence according to claim 1 characterized by the mutations 1541 T, 1568 T, 1633 G and 1666 C.
9. (Currently amended) A method for determining dispositions to hypertension diseases wherein the DNA of a proband is extracted and analyzed for sequence variations, and is compared with at least one similarly analyzed reference DNA sequence, wherein the reference DNA sequence comprises a base substitution at one or more positions selected from the group consisting of positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, 1839, 2110, 2640 2826, wherein the presence of mutation at one or more of the positions indicates a predisposition to hypertension, and wherein the method comprises the steps of:
  - i. hybridizing at least one pair of primers to genomic DNA comprising the beta2-adrenergic receptor gene according to SEQ ID NO: 1 under conditions suitable for performing PCR;
  - ii. amplifying one or more genomic sequences by PCR;
  - iii. analyzing the amplified sequences to discern differences between the proband and reference DNAs.
10. (Currently amended) Method according to claim 9 wherein the DNA of a proband is extracted and genotyped genotyped at least in position 1633.

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11. (Currently amended) Method according to claim 9 wherein the DNA of a proband is extracted and genotyped genotyfied at least in the three positions 1541, 1633 and 1666.
12. (Currently amended) Method according to claim 9 wherein the DNA of a proband is extracted and genotyped genotyfied at least in the four positions 1541, 1568, 1633 and 1666.
13. (Currently amended) Method according to claim 9 wherein the DNA of a proband is extracted and genotyped genotyfied at least in the seven positions 245, 565, 934, 1541, 1568, 1633 and 1666.
14. (Currently amended) Method according to claim 9 wherein the positions 1541, 1568, 1633 and 1666 are genotyped genotyfied.
15. (Currently amended) Method according to claim 14 wherein at least 3 of the 4 positions 1541, 1568, 1633 and 1666 are genotyped genotyfied.
16. (Currently amended) Method for determining the disposition to hypertension dispositions to diseases according to the claim 9, wherein the positions 1541, 1633 and 1666 are genotyped genotyfied.
17. (Currently amended) Method according to one of the claim 9 wherein genotyping genotyfying is brought about by sequencing or other methods suited for detecting variants.
18. (Currently amended) Methods according to ~~one of the~~ claim 9 for determining a disposition to high blood pressure and deviations of the blood pressure from the standard, ~~and other cardiovascular diseases including myocardial infarction and apoplexy; for determining a disposition to neuropsychiatric diseases selected from the group consisting of such as depression, anxiety syndromes, attention deficit disorder with hyperactivity, eating disorder, e.g. anorexia nervosa and bulimia or disorders caused by post traumatic stress; for determining a~~

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~~disposition to diseases of the autonomic nervous system such as e.g. Bradbury-Eggleston, Sjögren-Dräger and Riley-Day syndromes and dispositions to selective noradrenergic and baroreceptors or migraine; for determining a disposition to allergic diseases, in particular asthma and atopic disorder; for determining a disposition to metabolic diseases such as obesity and family "morbid obesity", including a prediction of the weight area as such or a disposition to a change of weight, including a prediction of the proportion of the measurements of the body as such as expressed e.g. in the "body mass index" (BMI).~~

19. (Currently amended) Method according to one of the claim 9 for determining an individually different reactivity of the autonomic nervous system, in particular to endogenous and exogenous stress.
20. (Previously presented) Method according to claim 19 for determining an individually different disposition to modification/deflections of blood pressure and/or heart rate caused by endogenous and exogenous stress or an individually different sensitivity/resistance to salt.
21. (Currently amended) Method according to one of the claim 9 for determining the course and the degree of severity of hypertension, diseases such as e.g. mentioned in claim 18, e.g. of neuropsychiatric diseases such as depression and anxiety syndromes, of cardiovascular diseases including myocardial infarct and apoplexy, of diseases of the autonomic nervous system and allergic diseases such as e.g. asthma.
22. (Withdrawn) Method according to one of the claim 9 for determining a disposition to metabolic diseases such as obesity.
23. (Currently amended) Method according to one of the claim 9 for predicting the survival time after severe diseases selected from the group consisting of such as after a myocardial infarct, stroke, cardiac failure and/or apoplexy.
24. (Canceled)

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25. (Canceled)

26. (Canceled)

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Canceled)

31. (Canceled)

32. (Canceled)

33. (Canceled)

34. (Currently amended) A human beta2-adrenergic receptor genomic DNA polynucleotide sequence variant determined by the method of claim 9, wherein the polynucleotide sequence variant comprises a base substitution at one or more positions of a reference DNA sequence, the positions being selected from the group consisting of positions 159, 245, 565, 934, 1120, 1221, 1541, 1568, 1633, 1666, 1839, 2078, 2110, 2640 and 2826.

35. (Currently amended) A polynucleotide sequence variant of claim 34 comprising one or more base substitutions selected from the group consisting of:  
(i) at position 159, T→A;  
(ii) at position 245, A→G;  
(iii) at position 565, G→A;

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- (iv) at position 934, G→A;
- (v) at position 1120, G→C;
- (vi) at position 1221, C→T;
- (vii) at position 1541, C→T;
- (viii) at position 1568, T→C;
- (ix) at position 1633, A→G;
- (x) at position 1666, C→G;
- (xi) at position 1839, G→A;
- (xii) at position 2078, C→T;
- (xiii) at position 2110, C→A;
- (xiv) at position 2640, G→C; and
- (xv) at position 2826, G→A.

36. (Currently amended) The genomic DNA variant determined by the method of claim 9, wherein the polynucleotide sequence variant comprises one or more substitutions selected from the group consisting of a T at position 1541, an A at position 1633, and a C at position 1666.
37. (Withdrawn) The genomic DNA variant determined by the method of claim 9, wherein the variant comprises one or more substitutions selected from the group consisting of a C at position 1541, a G at position 1633, and a G at position 1666.
38. (Withdrawn) The genomic DNA variant determined by the method of claim 9, wherein the variant comprises one or more substitutions selected from the group consisting of a T at position 1541, a G at position 1633, and a C at position 1666.
39. (Currently amended) The genomic DNA variant determined by the method of claim 9, wherein the polynucleotide sequence variant comprises one or more substitutions selected from the group consisting of a T at position 1541, T at 1568, A at position 1633, and C at position 1666.
40. (Withdrawn) The genomic DNA variant determined by the method of claim 9,

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wherein the variant comprises one or more substitutions selected from the group consisting of a C at position 1541, C at position 1568, G at 1633 and G at position 1666.

41. (Withdrawn) The genomic DNA variant determined by the method of claim 9, wherein the variant comprises one or more substitutions selected from the group consisting of a T at position 1541, T at position 1568, G at 1633 and C at position 1666.
42. (Previously presented) The sequence of claim 1, further comprising base substitutions at one or more positions selected from the group consisting of positions 1633, 1666 and 2078.
43. (Currently amended) The polynucleotide sequence variant determined according to the method of claim 9, further comprising a base substitution at one or more positions selected from the group consisting of positions 1633, 1666 and 2078.

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**CONDITIONAL PETITION FOR EXTENSION OF TIME**

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefore. The Assistant Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

**ADDITIONAL FEE**

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.